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ORIGINAL RESEARCH

Antimicrobial susceptibility changes of *Escherichia coli* and *Klebsiella pneumoniae* intra-abdominal infection isolate-derived pathogens from Chinese intra-abdominal infections from 2011 to 2015

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Background: To explore the susceptibility trends of antimicrobials and resistance increase to antibiotics of *Enterobacteriaceae* isolated from patients in China with intra-abdominal infections (IAI) from 2011 to 2015.

Methods: MIC_{90} and MIC_{50} values of 12 commonly used antibiotics from *Escherichia coli* and *Klebsiella pneumoniae* isolated from IAI samples were determined.

Results: A total of 8,477 Gram-negative bacterial pathogens were collected from 21 medical centers in China. The majority of IAI isolate-derived pathogens were *E. coli* (3,854, 45.5%) and *K. pneumoniae* (1,670, 19.7%) of which 1,990 (23.5%) were consecutively collected from community acquired (CA) and 6,186 (73.0%) from hospital acquired (HA) IAIs. The drugs with the highest efficacy against *E. coli* and *K. pneumoniae* isolates derived from IAI samples were imipenem, ertapenem, amikacin and piperacillin-tazobactam. MIC_{90} values for piperacillin-tazobactam were 64 μg/mL in 2015 with fluctuations from 16–64 μg/mL through the years for *E. coli*, but were stable at ≥64 μg/mL from 2011 to 2015 for *K. pneumoniae* isolates. Susceptibilities to ertapenem, imipenem and amikacin were high for *E. coli* isolates throughout the study, but *K. pneumoniae* isolated from abscesses, colon and peritoneal fluid collected from medical and surgical ICUs showed an increasing trend of carbapenem resistance in 2015.

Conclusion: In 2015 there was a trend of enhanced carbapenem resistance, particularly for *K. pneumoniae* isolated from IAI samples obtained from patients in ICUs.

Keywords: MIC, *Enterobacteriaceae*, intra-abdominal infection, carbapenems, cefepime, piperacillin-tazobactam

Introduction

The Study for Monitoring Antimicrobial Resistance Trends (SMART) program was established in 2002 as a worldwide system to establish the susceptibilities to antibiotics of facultative anaerobic and aerobic Gram-negative bacteria in vitro. Various surveillance programs monitoring IAI pathogens have reported that the percentage of extended beta-lactamase (ESBL) producing bacteria have increased during the last decade particularly in Asia,[1,2] with the predominant pathogens being *K. pneumonia* and *E. coli*. The most recent studies recorded IAI pathogen susceptibilities of these *Enterobacteriaceae* to amikacin, carbapenems and piperacillin-tazobactam,[3–6] but also an increasing resistance to carbapenems.[6–9] However, there

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were differences in the resistance patterns according to the region of China studied,[10] and generally resistance was less for community acquired compared to nosocomial infections[11,12] while ICUs have been identified as a major source of resistant *Enterobacteriaceae* infections in hospitals.[13–15] In the current investigation, MIC_{50} and MIC_{90} values were analyzed in order to determine the resistance trends of *K. pneumoniae* and *E. coli* isolated from IAI patients to carbapenems (imipenem and ertapenem), cephalosporins (ceftriaxone, cefepime ceftazidime, cefotaxime and cefoxitin), a broad-spectrum β-lactam antibiotic plus a beta-lactamase inhibitor combination (piperacillin–tazobactam) drug, an aminoglycoside (amikacin) and 2 fluoroquinolones (levofloxacin and ciprofloxacin) between 2011 and 2015 in China.

Samples and methodology

Isolates obtained from IAI patients

The Human Research Ethics Committee of our hospital approved the study protocols (Et. Number: S-K238) and decided that patient consent was not required.

In total, 1,670 *K. pneumoniae* and 3,854 *E. coli* isolates were detected in IAI samples, with a total of 8,477 *Enterobacteriaceae* and non-*Enterobacteriaceae* present during surgery or in paracentesis specimens from 2011 to 2015 (2011, n=1,908; 2012, n=1,898; 2013, n=1,614; 2014, n=1,574; 2015, n=1,483) from 21 centers across 7 regions of China namely the north, northeast east, central China, Jiang-zhe region, south and southeast, with a range of 77 to 250 samples per year per hospital, which were consecutively collected. The majority of the IAI specimens were collected during surgery, including some paracentesis samples, and were taken from the appendix, gall bladder, small intestine, colon, rectum, pancreas, stomach, liver, peritoneal fluid and abscesses. Isolates were identified using local site procedures and then sent for analysis to the clinical microbiology laboratory of Peking Union Medical College Hospital and for re-identification using MALDITOF MS (Vitek MS, BioMérieux, France).

Any isolates that contained the same species and genus from a particular patient were excluded from the study. Pathogens were identified using the standard methodology adopted in each clinical microbiology laboratory carrying out the tests. Isolates were deemed community-associated (CA) and hospital-associated (HA), if found in a sample taken <48 h or >48 h after an individual was admitted to a hospital.[11]

Minimum inhibitory concentration determination method

Pathogen susceptibility to antibiotic tests was carried out at the Peking Union Medical College Hospital Center laboratory using customized MicroScan broth microdilution techniques between 2011 and 2014, and with the aid of a Trek Diagnostic System (Thermo Scientific) in 2015. Minimum inhibitory concentrations $(MIC)_{90}/MIC_{50}$ were determined using interpretations of susceptibility that were based on defined CLSI clinical breakpoints.[16] Isolates were exposed to ceftriaxone, cefepime, amikacin, ceftazidime, ertapenem, piperacillin–tazobactam, imipenem and levofloxacin as recommended by appropriate guidelines for the management and diagnosis of complex IAIs.[17] These drugs may be administered to hospitalized patients with IAIs caused by Gram-negative *K. pneumoniae* and *E. coli* pathogens. In addition, cefotaxime, cefoxitin and ciprofloxacin were included.

According to the Clinical and Laboratory Standards Institute methodology,[18] ESBL was confirmed if cefotaxime or ceftazidime MICs were ≥ 2 μg/mL and their MICs decreased ≥8 fold when used in combination with clavulanic acid (4 μg/mL).

For each MIC test batch, reference strains of *E. coli* American Type Culture Collection (ATCC) 25922 and *K. pneumonia* (ATCC 700603) were used as quality control strains. The results were analyzed only if the quality control test results fell within acceptable ranges.

Statistical analysis

SPSS ver. 21.0 (SPSS Inc., Chicago, US) was used to carry out all statistical analyses. The susceptibility or resistance rates of all the Gram-negative isolates combined were determined using appropriate breakpoints for each species. The trend was analyzed using a chi-squared trend test for susceptibility and resistance rates. A P-value <0.05 was considered to be a statistically significant difference.

Results

Distribution of all isolates from CA and HA in IAI infected patients

In total, 8,477 isolate-derived pathogens were collected from patients with IAI infections from 2011 to 2015, including non-*Enterobacteriaceae* and *Enterobacteriaceae* pathogens. Table 1 shows the basic demographic characteristics of the included patients.

Table 1 Demographic characteristics of the included patients

	Escherichia coli, n (%)	*Klebsiella pneumoniae*, n (%)	Overall
Total	3,854 (100.0)	1,670 (100.0)	5,524
Gender			
Male	2,235 (58.0)	1,029 (61.6)	3,264
Female	1,619 (42.0)	641 (38.4)	2,260
Age (years)			
0–18	150 (3.9)	29 (1.7)	179
19–60	2,078 (53.9)	854 (51.1)	2,932
61–80	1,403 (36.4)	701 (42.0)	2,104
>81	223 (5.8)	86 (5.2)	309
Region			
East (non-Jiangzhe area)	845 (21.9)	341 (20.4)	1186
East (Jiangzhe area)	554 (14.4)	325 (19.5)	879
Central	605 (15.7)	185 (11.1)	790
North	616 (16.0)	301 (18.0)	917
Northeast	516 (13.4)	260 (15.5)	776
South	467 (12.1)	192 (11.5)	659
Southwest	251 (6.5)	66 (4.0)	317

Most of the isolate-derived pathogens were *Enterobacteriaceae* including *K. pneumoniae* and *E. coli*, which accounted for 19.7% and 45.5% of all IAIs respectively, of which 1,990 (23.5%) were collected from CA and 6,186 (73.0%) from HA IAIs. The distribution trend of *E. coli* from 2011 to 2015 showed that the HA *E. coli* infection rates of IAI patients were more than double those of CA IAIs. Similarly, the incidence of HA IAIs caused by *K. pneumoniae* was more than 3 fold that of CA IAIs throughout the years of the study (Table 2).

Distribution of *K. pneumoniae* and *E. coli* IAIs in various tissues/organs and different Chinese hospital departments from 2011 to 2015

Next, we analyzed the distribution trends of *K. pneumoniae* and *E. coli* from IAI patients in a number of different departments and in various tissues and organs.

For *E. coli*, the majority of IAI isolate-derived strains were sampled in general surgery departments (60.00–76.00%) and some came, to a lesser extent, from general medical, followed by surgical ICUs and emergency rooms (Figure 1A). The major distribution of *E. coli* from IAI samples was found mainly in the gall bladder, with an increase from 2011 to 2015, followed by the peritoneal fluid and abscesses, but became less prevalent in abscesses through the years (Figure 1B).

For isolates infected with *K. pneumoniae*, a similar distribution trend was detected in IAI patients treated in different hospital departments (Figure 2A), but in parallel with a similar predominance of gall bladder and peritoneal fluid infections, *K. pneumoniae* caused IAIs occurred to a lesser extent than *E. coli* in the appendix and to a greater degree in liver infections (Figure 2B).

Prevalence of ESBL+ *K. pneumoniae* and *E. coli* strains in isolates from IAIs between 2011 and 2015

As shown in Figure 3, the distribution of ESBL+ *K. pneumoniae* and *E. coli* strains from obtained from HA IAIs was about 10% higher than ESBL+ isolates from CA IAIs between 2011 and 2014. Only CA *K. pneumoniae and E. coli* IAIs caused by ESBL+ strains were reduced between 2014 and 2015 (Figure 3).

Susceptibility of *K. pneumoniae* and *E. coli* collected from IAI samples from different hospital departments to ertapenem and imipenem between 2011 and 2015

The susceptibilities of *E. coli* isolated from IAIs to ertapenem and imipenem were over 80% in most hospital departments except medical ICUs, which showed lower susceptibility to ertapenem in 2015 compared to the previous 4 years.

Table 2 Distribution of isolates from hospital acquired (HA) and community acquired (CA) intra-abdominal infections

			2011	2012	2013	2014	2015	All
All, n (%)			1,908 (100)	1,898 (100)	1,614 (100)	1,574 (100)	1,483 (100)	8,477 (100)
CA			315 (16.5)	440 (23.2)	354 (21.9)	575 (36.5)	306 (20.6)	1,990 (23.5)
HA			1,523 (79.8)	1,387 (73.1)	1,205 (74.7)	939 (59.2)	1,132 (76.3)	6,186 (73.0)
Other*			70 (3.7)	70 (3.7)	55 (3.4)	60 (3.8)	45 (3.0)	300 (3.5)
Escherichia coli	Total n (%)		904 (47.4)	875 (46.1)	744 (46.1)	683 (43.4)	648 (43.7)	3,854 (45.5)
	CA	n (% of *E. coli*)	196 (21.7)	230 (26.3)	190 (25.5)	269 (39.4)	170 (26.2)	1,055 (27.4)
	HA	n (% of *E. coli*)	708 (78.3)	645 (73.7)	554 (74.5)	414 (60.6)	478 (73.8)	2,799 (72.6)
Klebsiella pneumoniae	Total n (%)		333 (17.5)	330 (17.4)	358 (22.2)	318 (20.2)	331 (22.3)	1,670 (19.7)
	CA	n (% of *K. pn*)	51 (15.3)	85 (25.8)	82 (22.9)	112 (35.2)	69 (20.9)	399 (23.9)
	HA	n (% of *K. pn*)	282 (84.7)	245 (74.2)	276 (77.1)	206 (64.8)	262 (79.2)	1,271 (76.1)
Other bacteria	n (%)		671 (35.2)	693 (36.5)	512 (31.7)	573 (36.4)	504 (34.0)	2,953 (34.8)

Note: *indicates not specified.

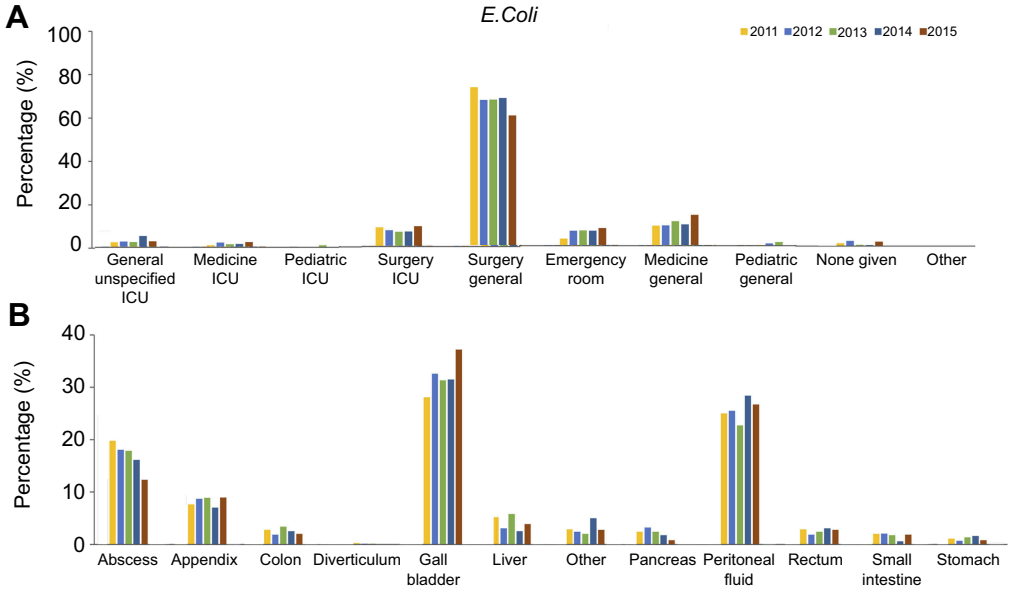

Figure 1 Distribution rate of *E. coli* isolates from IAI patients in (**A**) different departments and (**B**) tissues and organs of IAI patients.
Abbreviations: IAI, intra-abdominal infection; ICU, intensive care unit.

Similarly, susceptibilities of *K. pneumoniae* isolated from IAIs to ertapenem and imipenem were generally >80%, but with higher fluctuations throughout the years. Particularly in ICUs, susceptibilities to ertapenem dropped to <80% between 2011 and 2015, which was also the trend for imipenem (Figure 4).

Susceptibilities of IAI isolate-derived *E. coli* and *K. pneumoniae* strains from different tissues/organs to ertapenem and imipenem between 2011 and 2015

Susceptibility overall to *E. coli* was >80% for both ertapenem and imipenem in all tissues and organs, except for other sample sources in 2015, and for small intestine samples in 2014. However, beside some temporary fluctuations in the former years, particularly during 2015, the susceptibility of IAIs caused by *K. pneumoniae* fell in ertapenem and imipenem tests for samples obtained from abscesses, colon, peritoneal fluid and other sources (Figure 5).

Comparison of 11 commonly used antimicrobial agent resistances of *K. pneumoniae* and *E. coli* IAI isolate-derived pathogens from 2011 to 2015

Next, from 2011 to 2015 we analyzed the susceptibilities of IAI isolate-derived *K. pneumoniae* and *E. coli*

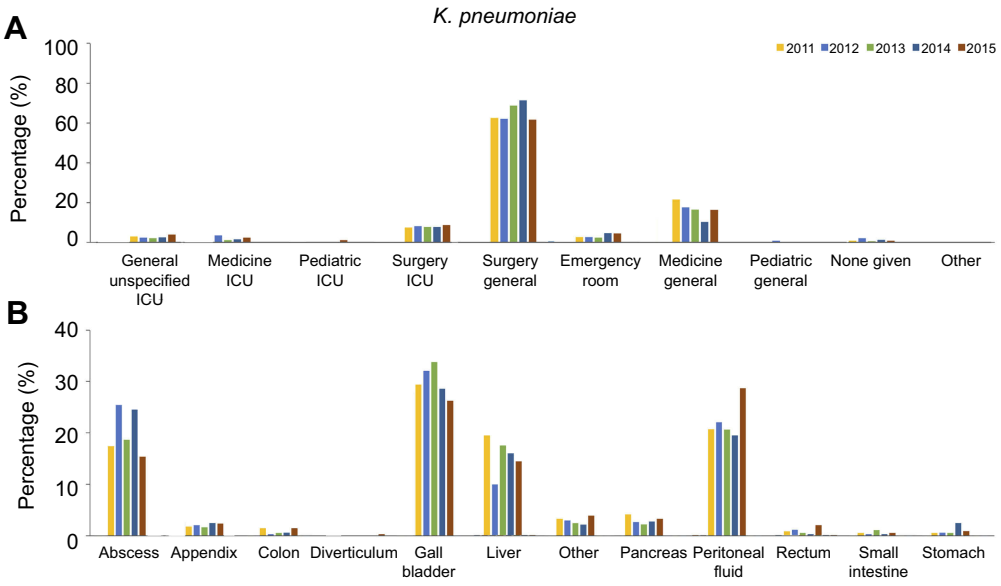

Figure 2 Distribution of *K. pneumoniae* isolates from IAI patients in (**A**) different departments, (**B**) tissues and organs.
Abbreviations: IAI, intra-abdominal infection; ICU, intensive care unit.

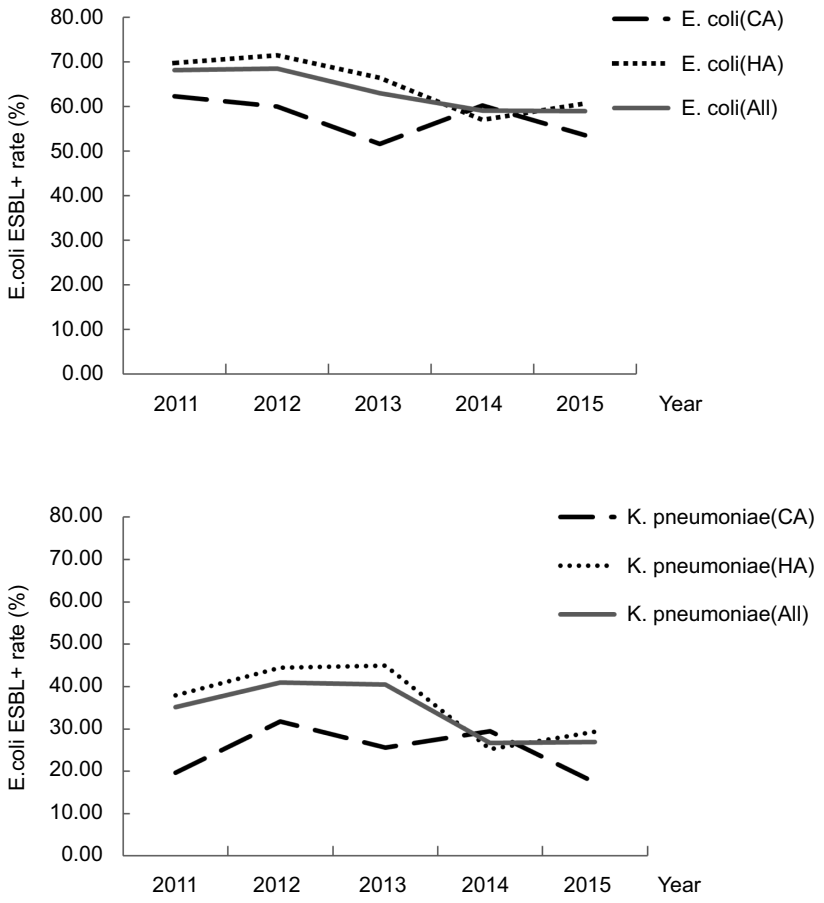

Figure 3 Distribution of extended beta-lactamase (ESBL)+ *E. coli and K. pneumoniae* isolates from HA and CA IAIs in 2011–2015.
Abbreviations: HA, hospital acquired; CA, community acquired; IAIs, intra-abdominal infections.

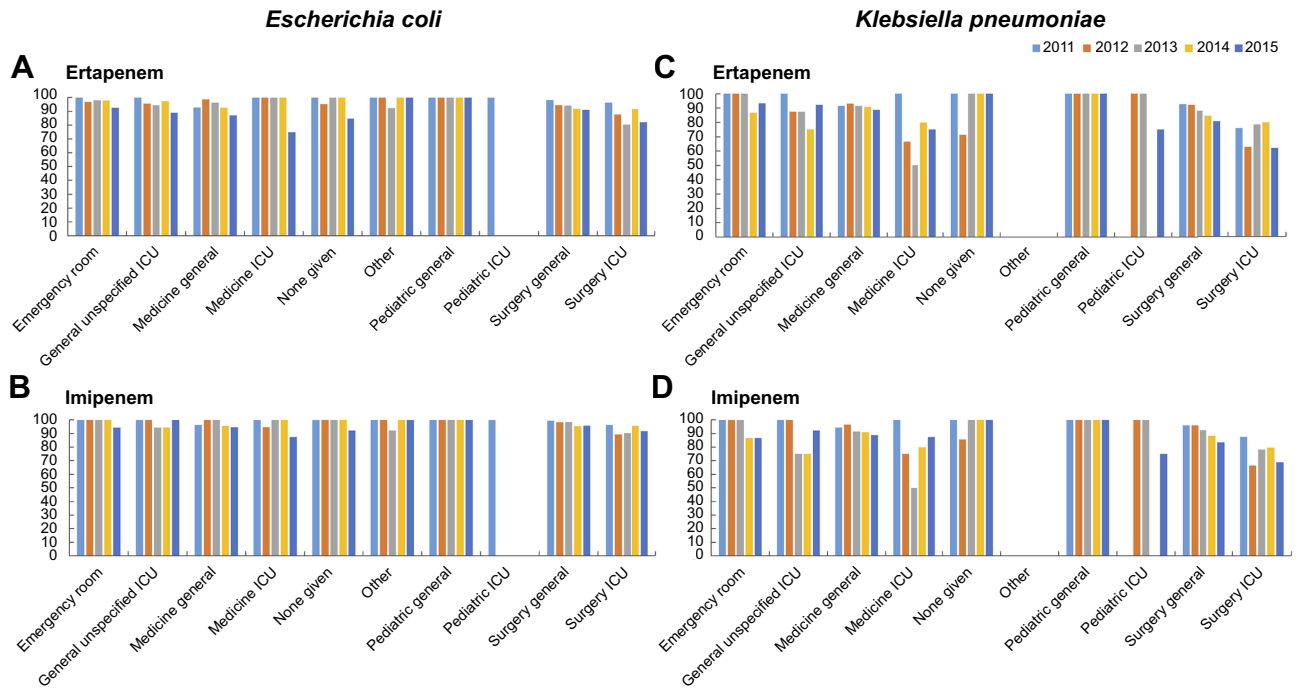

Figure 4 Susceptibilities of intra-abdominal infection isolate-derived pathogens sampled from various hospital departments. (**A**) Susceptibilities of *E. coli* to ertapenem and (**B**) to imipenem; (**C**) susceptibilities of *K. pneumoniae* to ertapenem and (**D**) to imipenem.

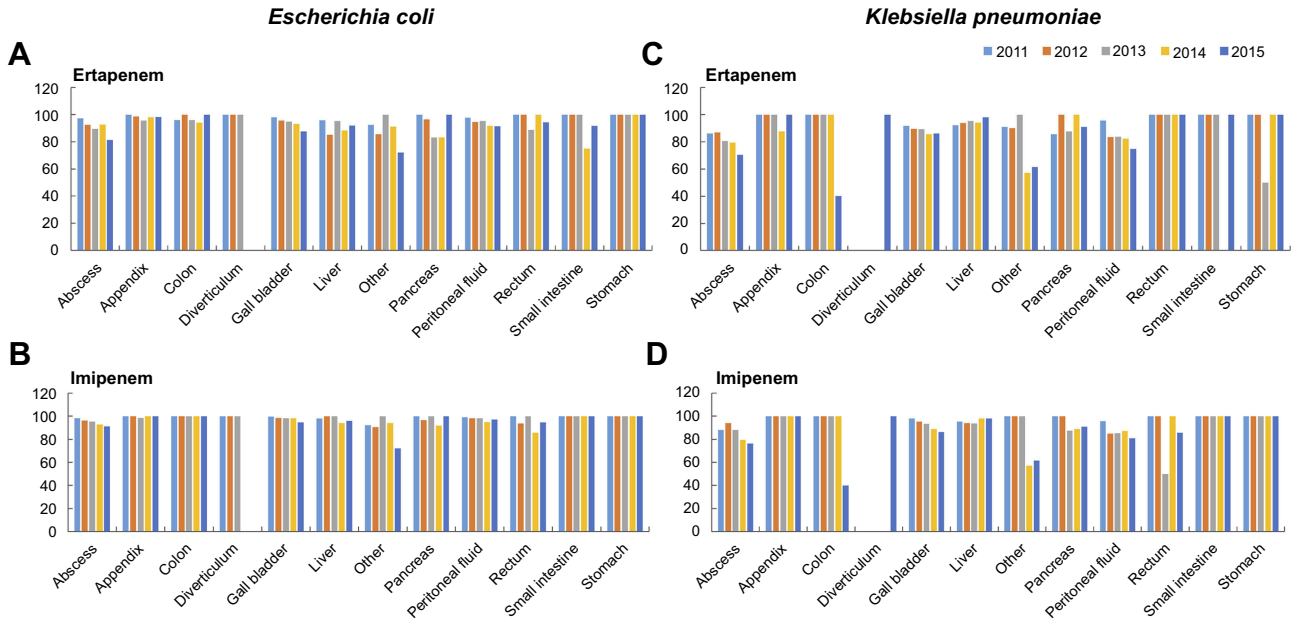

Figure 5 Susceptibilities of intra-abdominal infection isolate-derived pathogens sampled from various tissues and organs. (**A**) Susceptibilities of *E. coli* to ertapenem and (**B**) to imipenem; (**C**) susceptibilities of *K. pneumoniae* to ertapenem and (**D**) to imipenem.

IAI isolates to 11 commonly prescribed antimicrobial agents (Table 3). In general, *E. coli* was highly susceptible to amikacin (>90%) with few changes through the years and to the carbepenems, ertapenem and imipenem (both >89.2%), but since 2011, the resistance to carbapenems has shown a gradually increasing trend with higher MIC_{90} values. MIC_{90} and antibiotic-resistance values to the antimicrobial agent combination piperacillin/tazobactam also showed high susceptibilities against *E. coli*, but in 2015 the $MIC_{90,}$ MIC_{50} concentrations and resistance percentages were somewhat higher than in previous years.

Table 3 Susceptibility of *K. pneumoniae* and *E. coli* isolates obtained from intra-abdominal infections patients to 12 commonly prescribed antimicrobials from 2011 to 2015 (units: μg/mL)

Organism/ drug	2011				2012				2013				2014				2015			
	% S	% R	MIC_{50}	MIC_{90}	% S	% R	MIC_{50}	MIC_{90}	% S	% R	MIC_{50}	MIC_{90}	% S	% R	MIC_{50}	MIC_{90}	% S	% R	MIC_{50}	MIC_{90}
Escherichia coli (n=3,854)	**(n=904)**				**(n=875)**				**(n=744)**				**(n=683)**				**(n=648)**			
Amikacin	93.9	5.1	≤4	8	92.3	7.1	≤4	8	94.6	4.7	≤4	8	94.1	5.1	≤4	8	94.8	4.8	≤4	8
Cefepime	32.7	63.3	>32	>32	34.4	59.2	>32	>32	40.7	52.7	16	>32	40.3	55.5	32	>32	40.0***	49.4***	8	>32
Cefotaxime	28.9	70.6	>128	>128	29.7	69.8	>128	>128	35.0	64.3	>128	>128	36.3	63.1	>128	>128	33.2**	66.4**	>32	>32
Cefoxitin	73.5	13.5	4	>16	68.7	18.1	8	>16	76.1	15.1	4	>16	73.7	18.2	4	>16	65.1*	22.1***	8	>16
Ceftazidime	54.9	38.7	4	128	52.0	42.7	4	128	58.9	36.8	2	64	57.0	37.8	2	>128	56.8	34.0*	4	>32
Ceftriaxone	28.8	70.6	>32	>32	29.8	69.6	>32	>32	34.0	64.8	>32	>32	36.3	63.7	>32	>32	33.6**	65.9**	>32	>32
Ciprofloxacin	27.7	69.4	>2	>2	27.8	70.3	>2	>2	34.0	63.3	>2	>2	34.4	63.3	>2	>2	34.6***	64.0***	>2	>2
Ertapenem	97.8	1.7	≤0.03	0.25	94.7	2.9	≤0.03	0.5	94.0	4.0	≤0.03	0.5	92.8	4.4	≤0.03	0.5	89.2***	6.9 ***	≤0.03	1
Imipenem	99.0	1.0	0.12	0.25	97.9	1.3	0.12	0.25	98.1	1.3	0.12	0.25	95.8	2.9	0.12	0.5	95.1***	3.9 ***	≤0.5	1
Levofloxacin	32.3	62.3	>4	>4	30.2	62.4	>4	>4	37.5	53.5	>4	>4	38.8	54.3	>4	>4	35.8**	58.8**	>4	>4
Piperacillin Tazobactam	91.3	5.4	≤2	16	89.0	6.4	≤2	32	92.2	5.5	≤2	16	87.4	9.7	≤2	64	86.1**	9.9 ***	4	64
Klebsiella pneumoniae (n=1,670)	**(n=333)**				**(n=330)**				**(n=358)**				**(n=318)**				**(n=331)**			
Amikacin	92.5	7.5	≤4	≤4	92.1	7.9	≤4	8	93.3	6.2	≤4	8	91.2	8.5	≤4	8	86.1**	13.6**	≤4	>32
Cefepime	66.1	29.4	≤0.5	>32	57.9	35.5	≤0.5	>32	62.6	29.1	≤0.5	>32	67.9	28.9	≤0.5	>32	60.1	32.6	≤1	>32
Cefotaxime	60.4	38.7	≤0.5	>128	55.8	43.6	≤0.5	>128	55.0	43.6	≤0.5	>128	66.7	33.3	≤0.5	>128	55.6	43.2	≤0.5	>32
Cefoxitin	79.6	15.9	4	>16	73.6	20.3	4	>16	69.8	22.6	≤2	>16	73.0	22.6	≤2	>16	67.7**	27.8***	4	>16
Ceftazidime	74.8	22.5	≤0.5	128	69.7	27.6	≤0.5	128	72.1	24.6	≤0.5	128	74.5	22.6	≤0.5	128	65.9	29.6	≤0.5	>32
Ceftriaxone	59.8	39.3	≤1	>32	53.9	45.5	≤1	>32	55.0	43.3	≤1	>32	66.0	34.0	≤1	>32	55.9	43.2	≤1	>32
Ciprofloxacin	69.4	27.9	≤0.25	>2	67.3	27.0	≤0.25	>2	63.4	30.7	0.5	>2	72.6	25.8	≤0.25	>2	65.3	30.8	≤0.25	>2
Ertapenem	91.9	6.0	≤0.03	0.5	88.8	9.7	≤0.03	1	88.0	9.5	≤0.03	1	84.9	13.2	≤0.03	>4	81.6***	16.6***	≤0.03	>4
Imipenem	95.5	3.3	0.25	1	93.0	6.4	0.25	1	90.8	7.5	0.12	1	87.7	11.0	0.25	8	84.0***	13.6***	≤0.5	>32
Levofloxacin	73.9	20.7	≤0.5	>4	75.8	19.4	≤0.5	>4	72.1	22.9	≤0.5	>4	76.4	19.8	≤0.5	>4	68.3	28.1*	≤0.5	>4
Piperacillin Tazobactam	85.9	11.1	≤2	>64	84.9	11.2	≤2	>64	85.5	10.6	≤2	>64	82.4	14.5	≤2	>64	77.0**	19.9***	4	>64

Notes: The trend of susceptibility and resistance rates was analyzed with a chi-squared test. *P<0.05; **P<0.01; ***P<0.001.

Abbreviations: S, susceptibility; R, resistance; MIC, minimum inhibitory concentrations.

In addition, although in 2015 the drugs with the greatest efficacy against *K. pneumoniae* isolated from IAI samples were imipenem, ertapenem and amikacin (84.00%, 81.6% and 86.1%, respectively), the resistance of *K. pneumoniae* isolates gradually increased from 2011 to 2015, with a parallel decline of MIC_{50} and MIC_{90} concentrations to these drugs.

Discussion

A global study revealed that IAIs constituted 19.6% of all infections in ICUs and the mortality was higher than those caused by other infections (29.4% vs 24.4%, $P<0.001$), though most patients were treated with antibiotics (98.1%). However, only for two-thirds of these patients were microbial cultures reported,[19] indicating that empirical antimicrobial treatments are commonly applied in clinical practice underlining the importance of local antimicrobial susceptibility data. In the present study, we explored the susceptibility trends of *E. coli* and *K. pneumoniae* isolated from IAI patients from 2011 to 2015, which accounted for 46.1% and 22.2%, respectively of all consecutively collected samples, indicating that these *Enterobacteriaceae* were the predominant pathogens of IAIs, a finding in accordance with previously published literature.[20] The majority of *K. pneumoniae* and *E. coli* specimens were obtained during general surgery and the sources were mainly from peritoneal fluid, abscesses and the gall bladder, but IAIs caused by *K. pneumoniae* occurred to a lesser extent in the appendix and to a greater degree in liver infections compared with *E. coli*. This change has been attributed in the literature to an increased incidence of *K. pneumoniae*-induced pylephlebitis.[21] In general, MIC_{90} values were often ≥32 μg/mL, particularly for cefepime in *K. pneumoniae* and *E. coli* strains isolated from IAIs, although fluctuations were detected mainly for *K. pneumoniae*. Similar but more pronounced trends were found for piperacillin–tazobactam MIC_{90}s. The ESBL rates dropped in the years after 2013 particularly for *K. pneumoniae* strains isolated from IAIs, but this trend was not reflected in lower resistance rates to cephalosporins especially during 2015. Since also the resistance rate to cefoxitin, which is used for ESBL producer raised in 2015 other mechanisms like AmpC overexpression and porin loss might have developed.[22]

There was a trend of an increasing ertapenem MIC_{90} for *E. coli* from 0.5 to 1 and from 0.25 to 1 for imipenem between 2013 and 2015, which is in line with a previous study on Asian intra-abdominal and urinary tract infections, with reported imipenem and ertapenem MIC_{90} values for *Enterobacteriaceae* of 1 between 2013 and 2015. However, the MIC_{90} values of ertapenem (>4) and imipenem (8 to >32) for *K. pneumoniae* isolated from IAIs in our 2014–2015 study were higher than the reported values of 0.25 and 0.5 by Karlowsky and colleagues.[4]

MIC_{90} values of imipenem for *K. pneumoniae* reached ≥32 μg/mL, particularly in abscesses, colon and peritoneal fluid samples in 2015, which were collected from medical, surgical ICUs and general surgery departments. Especially for ICUs, a high incidence of carbapenem resistant *K. pneumoniae* infections have also been reported in other studies.[23,24] However, a general trend of increasing carbapenem resistant *K. pneumoniae* stains has been described for China in 2014.[25]

The trend of increasing carbapenem MICs for *K. pneumonia* is similar to vancomycin MICs for *Staphylococcus aureus* in recent years, particularly in Asia, a finding attributed to excessive use of vancomycin, which might also be the case for *K. pneumoniae* strains that were resistant to imipenem[26–29] However, the trend of a rising resistance of *K. pneumoniae* to carbapenem, particularly in ICUs, should be closely monitored, a finding that is in close agreement with previous reports in the literature.[30–32]

Conclusion

For the treatment of *E. coli*-induced IAIs, imipenem and ertapenem are still an option although the MIC_{90} values increased above the sensitivity level of 0.5–1 μg/mL, but they were still not in the resistance ranges of ≥2 and 4 μg/mL. In contrast, *K. pneumoniae* isolates derived from IAIs became predominantly resistant to ertapenem and imipenem, particularly during 2014 and 2015.

Ethics approval and consent to participate

The protocol has been reviewed by the human research ethics committee of the Institutional Review Board (IRB) of the Peking Union Medical College Hospital and since the project falls under the category observational study and all bacterial strains were from residual samples used in clinical diagnosis or were strains from their subcultures, it has been determined to meet the criteria for exemption. This project does not involve any patient information nor does it affect the normal diagnosis and treatment of patients, and after consultation with the IRB, formal ethical approval was reviewed and waived and written patient consent was not required (Ethics Approval Number: S-K238).

Availability of data and materials

The data that support the findings of this study are directly available from MSD China, but the SMART database is not in the public domain. Data are also available from the authors upon reasonable request and with permission of MSD China.

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Author contributions

All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

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